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09/674,779	01/03/2001	Jean-Louis Ruelle	BM45311	5330

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EXAMINER
BASKAR, PADMAVATHI

ART UNIT	PAPER NUMBER
1645	17

DATE MAILED: 08/13/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

File Copy

Office Action Summary	Application No. 09/674,779	Applicant(s) RUELLE, JEAN-LOUIS
	Examiner Padmavathi v Baskar	Art Unit 1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 January 2003 and 19 May 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27-29,31,34,35,53 and 62-64* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27-29,31,35,53 and 62-63* is/are rejected.

7)☒ Claim(s) *34 and 64* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *13* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Response to Amendment

1. The amendments filed on 1/29/03 (paper # 14) and new sequence listing filed on 5/19/03 (paper # 16) have been entered into the record. Claim 54 has been canceled. Claims 27, 34 and 53 have been amended. New claims 62-64 have been added. Claims 27-29, 31, 34-35, 53 and 62-64 are pending in the application.

Priority

2. This application is a 371 OF PCT/EP 99/03038, 05/3/1999, which claims priority under 35, U.S.C. 119 (a)- (d) to U.K 9809683.7, 05/06/1998.

In response to first action on merits, Applicant noted that the sequence listing submitted on disc in the instant application (2/12/02) was incorrect and submitted a new sequence listing containing SEQ.ID.NO: 1-14 on 5/19/03, Paper #. 16. Since the specification and the priority documents disclose the same sequences SEQ.ID.NO: 1-14, the new sequence listing containing SEQ.ID.NO: 1-14 has been entered in to the record.

Examiner has reviewed all the priority documents and found that the SEQ.ID.NO: 2 containing 172 amino acids in the present application was disclosed in the priority documents, PCT/EP 99/03038 and U.K 9809683. Therefore, this application gets priority as of filing date 5/6/1998 of the priority document for claims 27-29, 31, 34-35, 53 and 62-64 with respect to SEQ.ID.NO: 2

3. The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

Drawings

4. The drawings are objected to by the draftsperson under 37 C.F.R. 1.84 or 1.152. See attached PTO-948 for details. Applicant is required to submit a proposed drawing correction in

reply to this Office action. Failure to timely submit the proposed drawing correction will result in the abandonment of the application. MPEF 6.27.

It is noted that the figures 6 and 8 do not show the reactivity of Western-blot analysis (please see the attached figures 6 and 8) of recombinant protein probed with either anti-recombinant protein sera or pooled human convalescent sera bind to the antibody where as figure 7 clearly shows whole cell lysates of 16 strains of *M.catarrhalis* reacted (band around 17kD) with pooled sera against the recombinant BASB19 protein.

Further, "BSAB" is misspelled in the title. Therefore, applicant is required to submit corrected drawings for examination.

Information Disclosure Statement

5. Information Disclosure Statement filed on 1/29/03 (Paper # 13) is acknowledged and a signed copy is attached to this Office action.

Rejections withdrawn

6. In view of cancellation of claim 54 and amendment to the Claim 53 the rejection under 35 U.S.C. 112, first paragraph (for vaccine composition) is withdrawn

7. In view of amendment to the Claim 27, the rejection under 35 U.S.C. 112, second paragraph is withdrawn.

8. In view of according priority date as of 5/6/1998, the rejection of claims 27-29, 31, 53 under 35 U.S.C. 102(a) as being anticipated by Legace et al 2000 WO 007896 is withdrawn.

Rejections Maintained

9. The rejection of claims 27-29, 31, 35, 53 and newly added claims 62-63 under 35 U.S.C. 102(b) as being anticipated by Helminen et al 1994 (J.Infec.Dis, 170; 867-872) is maintained as set forth in the previous office action.

Claims are directed to an isolated polypeptide comprising (a) an amino acid sequence SEQ.ID.NO: 2 (b) an immunogenic fragment of SEQ.ID.NO: 2 where in the immunogenic fragment comprises 15, 20, 47-59 and 158-172 of SEQ.ID.NO: 2, wherein said polypeptide induces an immune response.

Helminen et al 1994 disclose an isolated polypeptide, outer membrane protein i.e., OMP from whole cell lysate of *M.catarrhalis*. Monoclonal antibodies were produced by administering (i.e., immunizing) whole cell lysate antigens to mice (page 867, right column through page 868, left column, first paragraph). Applicant's use of the open-ended term "comprising " in the claims 27-29 and 31 fails to exclude unrecited steps or ingredients and leaves the claims open for inclusion of unspecified ingredients, even in major amounts. Therefore, the claims read on the disclosed isolated polypeptide, OMP from *M.catarrhalis*. Whole cell lysates from *M.catarrhalis*. inherently comprise the amino acid sequence as set forth in the SEQ.ID.NO: 2 and fragments of SEQ.ID.NO: 2. See In re Horvitz, 168 F 2d 522, 78 U.S.P.Q. 79 (C.C.P.A. 1948) and Ex parte Davis et al., 80 U.S.P.Q. 448 (PTO d. App. 1948). In the absence of evidence to the contrary the disclosed prior art protein and the claimed isolated polypeptide comprising (a) an amino acid sequence matching SEQ.ID.NO: 2 are the same. Since the Office does not have the facilities for examining and comparing applicants' claimed isolated polypeptide comprising SEQ.ID.NO: 2 with the polypeptide of prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Applicants' arguments filed on 1/29/03 have been fully considered but they are not deemed to be persuasive.

Applicant states that the recited prior art of record does not anticipate the claimed invention and cites MPEP 2131 for support. Applicant states that Helminen et al disclose UspA1 peptide and is not very similar to BASB019 protein.

It is the position of the examiner's position that applicant failed to show that the disclosed outer membrane proteins do not contain an isolated polypeptide comprising SEQ.ID.NO: 2. The use of open-ended term "comprising in the claims fails to exclude unrecited steps or ingredients and leaves the claims open for inclusion of unspecified ingredients, even in major amounts See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594. The examiner rejected the claims based on inherency since the outer

membrane proteins contain several proteins that include isolated polypeptide comprising SEQ.ID.NO: 2 and other M.catarrhalis antigens.

There is nothing on the record to show the differences between the claimed isolated polypeptide comprising SEQ.ID.NO: 2 and the disclosed outer membrane proteins. Therefore, the prior art reads on an isolated polypeptide comprising a member selected from the group consisting of (a) the amino acid sequence SEQ.ID.NO: 2. Further, it is the position of the examiner that the applicant is arguing the limitation such as "BASB019 protein" etc which is not set forth in the claims. Thus, the prior art anticipates the claimed invention.

New Rejections Based on Amendment

Claim Rejections - 35 USC 112

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 27- 29,31, 35, 53 and 62-63 are rejected under 35 U.5.C. 112, first paragraph, because the specification, while being enabling for an isolated polypeptide consisting of the amino acid sequence SEQ ID NO: 2, fusion protein comprising the amino acid sequence SEQ ID NO: 2, an immunogenic composition comprising the amino acid sequence SEQ ID NO: 2 and a pharmaceutically accepted carrier, an isolated polypeptide consisting of the immunogenic fragment of amino acids 47-59 of SEQ.ID.NO: 2 and an isolated polypeptide consisting of the immunogenic fragment of amino acids 158 - 172 of SEQ.ID.NO: 2 does not reasonably provide enablement for an isolated polypeptide comprising [redacted] immunogenic fragments of 15 amino acids, 20 amino acids of SEQ.ID.NO: 2. The specification does not enable

any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are drawn to an isolated polypeptide comprising SEQ.ID.NO: 2, immunogenic fragment comprises at least 15 amino acids and 20 amino acids of SEQ.ID.NO: 2. Claims are also drawn to a fusion protein and immunogenic composition comprising said fragments, pharmaceutically acceptable carrier.

The specification broadly describes as part of the invention, an isolated protein of SEQ ID NO: 2, which is encoded by BASB 019 gene from M.catarrhalis, ATCC strain 43617. The specification also teaches on pages 47-48 that this full-length protein contains 172 amino acids. The actual biological function of the protein represented as SEQ ID NO: 2 is not set forth in the specification although it is a recombinant protein from pathogenic bacteria. The specification fails to teach all fragments of 15 amino acids and 20 amino acids of SEQ.ID.NO: 2.

The isolated polypeptide comprising of SEQ ID NO: 2 is uncharacterized by this specification and is not asserted to belong to any known family of proteins. The specification discloses the claimed polypeptide as an immunogen (page 67) and formulating the compositions in Freund's adjuvant to immunize rabbits for preparing antibodies. However, the specification fails to teach and guide an isolated polypeptide comprising all immunogenic fragments of 15 or 20 amino acids of SEQ.ID.NO: 2 have the ability to bind to an antibody raised against full-length protein. Moreover, protein chemistry is probably one of the most unpredictable areas of biotechnology and the art teaches that the significance of any particular amino acid sequences (i.e. fragments) for different aspects of biological activity cannot be predicted a priori and must be determined empirically on a case-by-case basis (Rudinger et al, in "PEPTIDE HORMONES", edited by Parsons, J.A., University Park Press, June 1976, page 6). The art specifically teaches that even a single amino acid change in a protein leads to

unpredictable changes in the biological activity of the protein. For example, replacement of a single lysine residue at position 118 of the acidic fibroblast growth factor by glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological-activity of the protein (Burgess et al., The Journal of Cell Biology, 111:2129-2138, 1990). In transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine, or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biologic activity of the mitogen (Lazar et al., Molecular and Cellular Biology, 8(3): 1247-1252, 1988). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification, will often dramatically affect the biological activity of a protein. Proteins with replacement of single amino acid residues may lead to both structural and functional changes in biological activity and immunological recognition. For example, Jobling et al. (Mol. Microbiol. 1991, 5(7): 1755-67 teach a panel of single amino acid substitutions by oligonucleotide directed mutagenesis in proteins and such proteins differ in native conformation, immunological recognition, binding and toxicity, thus exemplifying the importance of structural components to both biological function and immunological recognition. The specification fails to teach the relevant identifying characteristics of a representative number of SEQ.ID.NO: 2 fragments, sufficient to allow one skilled in the art to determine the function of the fragments. In view of the unpredictability of the art, the lack of teachings of the specification, it would require undue experimentation on the part of the skilled artisan to practice the invention as claimed.

12. Claims 34 and 64 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Status of Claims

13. No claims are allowed.

Conclusion

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP ' 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padma Baskar whose telephone number is (703) 308-8886. The examiner can normally be reached on Monday through Friday from 6:30 AM to 4 PM EST

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Padma Baskar Ph.D.

8/5/03

LYNETTE R. F. SMITH
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